

Remarks

Consideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 35-68 are pending in the application, with 35 being the sole the independent claim. Claim 35 has been amended in order to more clearly define the subject matter of the claimed invention. The amendment does not narrow the scope of the claim as it makes explicit, that which was implicit in view of the specification. Support for the amendment can be found at page 6, lines 1-10; page 8, lines 27-32; and page 10, lines 6-11 of the specification and Example 1. The amendment does not add new matter.

The specification has also been amended. The amendment to the specification does not add new matter. According to the M.P.E.P., identification of a trademark by scientific or other explanatory language may be introduced by amendment, if restricted to the characteristics of the product known at the time the application was filed to avoid any question of new matter. M.P.E.P. § 608.01(v). The phrase "random-branched" provides an identifying physical characteristic of the PEI products listed in the specification. This characteristic of the product was known at the time the application was filed.

In addition, the phrase "random-branched" provides an inherent physical characteristic of the PEI products provided in the specification. Under established case law, inherent physical properties of a compound can be amended into the specification after the filing date without adding new matter to the disclosure. *See, e.g., Kennecott Corp. v. Kyocera Int'l Inc.*, 5 USPQ2d 1194 (Fed. Cir. 1987). "Random-branched" structure is an inherent physical characteristic of the PEI products listed in the specification at page 6, that was known to those skilled in the art at the time of filing.

Accordingly, the amendment does not add new matter.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Rejections Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 35-43, 49 and 65 under 35 U.S.C. § 102(e) as allegedly being anticipated by either one of Yin *et al.* (U.S. Pat. No. 5,919,442) or Tomalia *et al.* (U.S. Pat. No. 5,714,166). Applicants respectfully traverse the Examiner's rejection.

In Applicants' previous response, Applicants asserted that the term "PEI," when used alone and without any modifying adjective or other descriptive term, is recognized in the art to mean random-branched PEI, which is the "regular" PEI that has been commercially available for a long time. To support this assertion, Applicants have provided a Declaration by one of ordinary skill in the art attesting to this fact. (*See Declaration of Manfred Ogris Under 37 C.F.R. § 1.132, page 2.*) Despite these assertions, the Examiner has alleged that "[t]he assertion that one of ordinary skill in the art would recognize PEI as meaning 'random branched chain' polyethyleneimine lacks support and is contradicted by Exhibits 3 and 4." (Office Action, page 14.)

The Examiner has asserted that Godbey *et al.* (Exhibit 3) contradict Applicants' assertion as to the art-recognized meaning of PEI. Applicants respectfully disagree. There is nothing in Godbey *et al.* that contradicts Applicants' assertions. As the Examiner correctly indicates, Godbey *et al.* teach that PEI comes in two forms: linear and branched. (Godbey *et al.*, page 150, column 1.) But Godbey *et al.* also teach that:

The branched form of PEI has yielded significantly greater success in terms of cell transfection, and is therefore the standard form of PEI that has been used for gene delivery. Unless otherwise noted, all references to PEI ascribe to the branched form of the molecule.

(*Id.* at column 2.)

Figure 1 of Godbey *et al.* show a structure of "Branched PEI." The structure is the random-branched form of PEI. In view of these teachings in Godbey *et al.*, Applicants assert that Godbey *et al.*, rather than contradicting Applicants' assertions, actually support Applicants' assertions about the meaning of the term "PEI" in the art of gene delivery. That is, one of ordinary

skill in the art would recognize the term to refer to the random-branched form of the polymer absent any modifying adjective or other descriptive term or phrase.

With respect to Klotz *et al.* (Exhibit 4), the Examiner is again correct in noting that Klotz *et al.* teach that PEI is a "highly branched water soluble polymer." (Klotz *et al.*, page 4753, column 1.) But Klotz *et al.* also provide a schematic representation of the "highly branched" PEI. The schematic representation shows the PEI as a random-branched polymer. Thus, the definition of PEI provided by Klotz *et al.* is not as broad as the Examiner suggests and would exclude the highly ordered, non-random forms of PEI disclosed by Yin *et al.* and Tomalia *et al.* Further, nothing in Klotz *et al.* contradicts Applicants' assertions of the art-recognized meaning of the term "PEI." After describing the general structure of the PEI, they note that the specific PEI used in their experiments was PEI-600. Applicants fail to see how these teachings contradict Applicants' assertion of the art-recognized meaning of the term "PEI."

However, in the interest of advancing prosecution, Applicants have amended the claims to further clarify any ambiguity that may exist as to the structure of the PEI claimed. The amendment makes explicit what was implicit in view of the specification and the understanding within the art. As amended, the claims are directed to complexes formed with "random-branched" PEI. Neither, Yin *et al.* nor Tomalia *et al.* teach the use of random-branched PEI. Thus, neither Yin *et al.* nor Tomalia *et al.* anticipate the claims. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has rejected claims 35, 41-45, 49, and 52 under 35 U.S.C. § 102(e) as allegedly being anticipated by Bogdanov *et al.* (U.S. Pat. No. 5,871,710). Applicants respectfully traverse the Examiner's rejection.

In response to Applicants' previous arguments, the Examiner has indicated that "[i]t is the position of the PTO that the term 'complex' is a generic term which encompasses both ionic and

covalent complexes." (Office Action of November 27, 2001, page 16.) Applicants respectfully disagree with the position taken by the PTO and note that the language of the claims are "not to be read in a vacuum, and limitations therein are to be interpreted in light of the specification." *In re Marosi*, 710 F.2d 799, 802 (Fed. Cir. 1983) (quoting *In re Okuzawa*, 537 F.2d 545, 548 (CCPA 1976)). Thus, it would be improper for the PTO to take a "position" on the meaning of word or phrase that would apply to all cases. The meaning of a term or a phrase must be interpreted in view of the teachings of the specification. Applicants assert that in view of the teachings of the specification, including Example 1, which teaches how to make the complexes of the claimed invention, it is clear that the term "complex" as used in claim 35 does not refer to covalent complexes.

However, in the interest of advancing prosecution, Applicants have amended claim 35 to make clear that the "complex" is not a covalent complex. Because Bogdanov *et al.* refer to covalent attachment of DNA to PEI, Bogdanov *et al.* do not teach every element of the claimed invention. Thus, Bogdanov *et al.* do not anticipate the claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 35, 42, 44-52, 54, 56-65, and 67-68 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Yin *et al.* (U.S. Pat. No. 5,919,442) or Tomalia *et al.* (U.S. Pat. No. 5,714,166), in view of one or more of the following references: Szoka (U.S. Pat. No. 5,661,025); Bogdanov *et al.* (U.S. Pat. No. 5,871,710); Mizushima *et al.* *Nucleic Acid Res.* 18(17): 5322 (1990); Sompayarac *et al.*, *PNAS USA* 78(12):7575-78 (1981); and Obaru *et al.*, *Human Gene Therapy* 7(18): 2203-2208 (1996). Applicants respectfully traverse the Examiner's rejection.

The defects of Yin *et al.*, Tomalia *et al.* and Bogdanov *et al.* have been described above. Neither Szoka, Mizushima *et al.*, Sompayarac *et al.*, nor Obaru *et al.* remedy the defects of Yin *et al.* and Tomalia *et al.* Accordingly, the cited references do not render unpatenable the claimed invention. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

The application has been amended as follows:

In the Specification:

The paragraph beginning at page 6, line 1:

Examples of commercially obtainable random-branched PEI with different molecular weights which is suitable within the scope of the present invention are PEI 700 D, PEI 2000 D, PEI 25000 D, PEI 750000 D (Aldrich), PEI 50000 D (Sigma) and PEI 800000 D (Fluka). BASF also market random-branched PEI under the brand name Lupasol® in different molecular weights (Lupasol® FG: 800 D; Lupasol® G 20 anhydrous: 1300 D; Lupasol® WF: 25000 D; Lupasol® G 20: 1300 D; Lupasol® G 35: 2000 D; Lupasol® P: 750000 D; Lupasol® PS: 750000 D; Lupasol® SK: 2000000 D).

In the Claims:

35. (Amended) Complexes of nucleic acid and random-branched polyethyleneimine (PEI), characterized in that the PEI is modified with a hydrophilic polymer covalently coupled thereto,

wherein said complexes are formed by (a) mixing solutions of nucleic acid and PEI and afterwards, covalently modifying the PEI with hydrophilic polymer or (b) mixing solutions of nucleic acid and PEI, which has been covalently modified with hydrophilic polymer before said mixing.